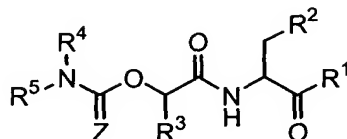


Abstract

This invention provides caspase inhibitors of formula **I**:



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wherein Z is oxygen or sulfur; R<sup>1</sup> is hydrogen, -CHN<sub>2</sub>, R, CH<sub>2</sub>OR, CH<sub>2</sub>SR, or -CH<sub>2</sub>Y; Y is an electronegative leaving  
10 group; R<sup>2</sup> is CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H, or esters, amides or isosteres thereof; R<sup>3</sup> is a group capable of fitting into the S2 subsite of a caspase enzyme; R<sup>4</sup> and R<sup>5</sup> are taken together with the intervening nitrogen to form heterocyclic ring and R is as described in the specification. The  
15 compounds are effective inhibitors of apoptosis and IL-1 $\beta$  secretion.